REMARKS

Favorable reconsideration is respectfully requested in view of the above amendments and following remarks. Claims 1 and 9 have been amended. The amendments to claims 1 and 9 are supported by the original specification, for example by page 3, lines 16-22. Claim 31 is new, and is supported, for example, by page 28, lines 14-18. Claims 1-2, 4-11 and 13-31 are pending. No new matter has been added.

Claim rejections - 35 U.S.C. § 103

Claims 1, 2, 4-11 and 13-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP1 002874 A2 (Komori et al.) in view of Eur. J. Biochem., 1996, Vol. 242, pp. 499-505 (Yoshida et al.) and further in view of Biochemistry, 1988, Vol. 27, pp. 5470-5476 (Montellano et al.) and further in view of US Patent No. 6,127,138 (Ishimaru et al.), and further in view US Patent No. 5,556,788 (Kwan et al.). Applicants respectfully traverse this rejection.

Claim 1 recites adding a degradation FAOD to the sample as a pretreatment so that a free amino acid that is glycated present in the sample as a contaminant is degraded and removed from the sample by the degradation FAOD and the analyte remains in the sample. According to the features recited by claim 1, the hydrogen peroxide generated from the free amino acid that is glycated present as a contaminant is not measured. As such, unwanted influence from free amino acids that are glycated formed from exogenous substances administered via an intravenous drip or the like can be eliminated, thereby improving the accuracy in the measurement of the glycated protein (page 2, line 34 to page 3, line 22).

The rejection refers to page 504 of Yoshida, and contends that the motivation taught by Yoshida would be the interference caused by the glycation of amino groups in the side chain of the amino acid residues of blood proteins other than the glycated protein to be measured. Applicants respectfully submit that the rejection's analysis of Yoshida is incorrect.

In particular, page 504 of the reference teaches that their enzymic measurement of glycated proteins is not specific for glycated albumin among glycated proteins, and as such, their enzymic measurement accounts for the total glycated serum protein. One of ordinary skill in the art would clearly understand from this description that Yoshida is indicating that the FAODs used in their enzymic method are unable to oxidize proteins directly, and as such, the enzymatic measurement of the glycated proteins must be preceded by a proteolytic

digestion to liberate the glycated amino acids within the proteins. What is measured then is the hydrogen peroxide generated from not only the liberated glycated amino acids from the glycated albumin, but also that of other glycated proteins. The resulting measurement thus is the total glycated serum protein, which Yoshida in fact indicates is a more sensitive indicator of great fluctuations of blood glucose as compared to glycated albumin. As such, contrary to the rejection's position, Yoshida is far from indicating that the glycation of amino groups in the side chain of amino acid residues of blood proteins other than the glycated protein to be measured is causing an "interference".

The rejection refers to paragraphs [0054] and [0061-0062], and contends that Komori teaches pretreatment with a measurement FAOD and adding a measurement FAOD during redox reaction and that the conditions of FAOD treatment are determined as appropriate on the type of FAOD used, and further contends that it would have obvious to use Yoshida's FAOD in Komori's method with a predictable result of degrading/removing a glycated amino acid as a contaminant present in the sample by the FAOD enzyme. Applicants respectfully submit that the rejection's analysis of the combination of the references is incorrect.

In particular, Komori teaches in paragraph [0005] that pretreatment with the tetrazolium compound removes the reducing substances that may reduce hydrogen peroxide. Yoshida teaches the use of FAODs that exhibit activities towards fructosyl-$^{\alpha}$N-valine and/or fructosyl-$^{\varepsilon}$N-lysine, the activities being the oxidative deglycation of fructosyl-$^{\alpha}$N-valine and/or fructosyl-$^{\varepsilon}$N-lysine to produce glucosone, valine and/or lysine and hydrogen peroxide. Thus, if Yoshida's FAODs are used in Komori's method as indicated in the rejection, then Yoshida's FAOD would catalyze the generation of hydrogen peroxide from fructosyl-$^{\alpha}$N-valine and/or fructosyl-$^{\varepsilon}$N-lysine present in the sample before the protease treatment, and the tetrazolium compound of Komori would remove any reducing substances that may have reduced the hydrogen peroxide generated from the above reaction. The references do not indicate that the hydrogen peroxide is removed at any point before the color developing redox reaction. Thus, the addition of the protease and measurement FAOD and the subsequent color developing redox reaction would measure the amount of hydrogen peroxide generated not only from the glycated protein, but also the amount of hydrogen peroxide generated from the fructosyl-$^{\alpha}$N-valine and/or fructosyl-$^{\varepsilon}$N-lysine present before the protease treatment. As such, contrary to the rejection's position, the expected result of the combination of Komori and

Yoshida would be that the hydrogen peroxide generated from the fructosyl-$^{\alpha}$N-valine and/or fructosyl-$^{\varepsilon}$N-lysine present in the sample before the protease treatment would be measured, and thus the glycated amino acids would have been acted upon by Yoshida's FAOD as an analyte, as opposed to a contaminant.

In fact, it can be clearly understood from Komori as a whole and Yoshida as a whole that both references are directed to using FAODs as part of an enzyme-based sensor that employs the FAOD in sensing a glycated amino acid as an analyte so that the amount of the glycated amino acid is measured. Thus, if the references were combined as described in the rejection, one would expect that the glycated components listed in paragraph [0029] of Komori including glycated amino acids within the sample would be measured. Nothing in the references teaches or suggests adding a degradation FAOD to the sample as a pretreatment so that a free amino acid that is glycated present as a contaminant in the sample is degraded and removed from the sample by the degradation FAOD and the analyte remains in the sample as recited in claim 1, so that the hydrogen peroxide generated from the free amino acid that is glycated present as a contaminant is not measured. Montellano, Ishimaru and Kwan do not remedy the deficiencies of Komori and Yoshida. Accordingly, claim 1 and the dependent claims therefrom are patentable over the references, taken alone or together.

The rejection contends that once the method of measuring an amount of glycated protein in an analyte was established, providing a measuring kit of claim 9 to determine the amount of the glycated protein would become obvious in view of Ishimaru et al. However, as discussed above, if Komori and Yoshida were combined as described in the rejection, one would expect that the glycated components listed in paragraph [0029] of Komori including glycated amino acids within the sample would be measured. Nothing in the references teaches or suggests using a pretreatment reagent containing a first FAOD that is present in an amount suitable for the degradation of a free amino acid that is glycated present in the sample as a contaminant as recited in claim 9. Accordingly, claim 9 and the dependent claims therefrom are patentable over the references, taken alone or separately.

Claim 31 is new, and recites that the pretreatment includes removing hydrogen peroxide formed from a redox reaction between the degradation FAOD and the free amino acid that is glycated. As indicated above, Komori in fact aims to remove any reducing substances that may reduce the hydrogen peroxide as a pretreatment, and as such, leads away

from the features of claim 31. Therefore, claim 31 is further removed from the references.

In view of the above, favorable reconsideration in the form of a notice of allowance is requested. Any questions or concerns regarding this communication can be directed to the attorney-of-record, Douglas P. Mueller, Reg. No. 30,300, at (612) 455.3804.

Respectfully submitted,

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